

**REMARKS**

In reply to the Office Action mailed August 21, 2008, Applicants amended claim 86 and cancelled claims 89 and 90. Claims 86, 94-98, 100-102 and 110-119 are pending and under examination. Please consider the following remarks.

**Summary of Telephone Conference with Examiner**

Applicants thank the Examiner for the courtesy of a telephonic interview on November 27, 2008, in which proposed amendments to claim 86 were discussed. Applicants agree with the substance of the interview as provided in the Examiner's interview summary mailed December 4, 2008.

**Rejections Under 35 U.S.C. §103**

The Examiner has maintained the rejection of claims 86, 89, 90, 94-98, 100-102 and 110-119 under 35 U.S.C. §103 as being unpatentable over Rana in view of Florence, "Manoharan I", and Cook and evidenced by "Manoharan II". Claim 86, the only pending independent claim, recites a double-stranded ribonucleic acid (dsRNA) comprising a complementary RNA strand, a sense RNA strand and only one lipophilic group having a  $\log K_{ow}$  exceeding 1. The complementary RNA strand has a nucleotide sequence which is complementary to a target RNA, and wherein the target RNA is an mRNA transcript of a target gene or of a (+) strand RNA virus. The lipophilic group is covalently attached to a 5'-end of the complementary RNA strand and a linkage between the lipophilic group and the 5'-end of the complementary RNA strand comprises a phosphodiester group.

Applicants have asserted in their reply to the previous office action that Rana teaches away from the 5' modification of the complementary RNA strand. (See Reply to Office Action of July 22, 2008.) Furthermore, as stated in the specification on page 17, line 24 to page 18, line 1, the inventors surprisingly found that 5'-modifications where the modifying group is linked to the 5'-end of the antisense strand via a phosphodiester group may very well function as RNA interference agents. In the outstanding Office Action, The Examiner acknowledges that "Applicant is correct in that Rana et al. teach the 5' end of the antisense strand should contain a free OH group for efficient RNA interference." (See Office Action, page 3.) However, the Examiner asserts that Rana does not teach away from modifications of the 5' end of the sense strand. Without conceding the merits of this assertion and solely for the purposes of expediting prosecution, Applicants have amended claim 86 to require that the lipophilic group be covalently

attached to a 5'-end of the complementary RNA strand. Applicants therefore request that the corresponding rejection be withdrawn.

Applicants submit the application is in condition for allowance, which action is requested.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 50/2762, referencing Attorney's Docket No. A2038-7052US.

Respectfully submitted,  
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